an urban academic medical center and randomized 156 patients to supervised treadmill exercise, lower extremity resistance training, or to a control group. The main outcome measures were a 6-minute walk performance and a short physical performance battery. Secondary outcomes were brachial artery flow–mediated dilatation, treadmill walking performance, scores on the Walking Impairment Questionnaire, and scores on the Short Form 35-Item Health Survey physical functioning (SF-36PF) questionnaire.

With respect to control groups, patients in the 6-minute walk who underwent supervised exercise training improved walking distance by 35.9 m ($P < .001$) and patients who received resistance training improved walking distance by 12.4 m ($P = .24$). Neither the treadmill group nor the resistance training group improved short form physical battery scores. Brachial artery flow–mediated dilatation improved by 1.53% in the treadmill group ($P = .02$) compared with controls. Compared with controls, the treadmill group had greater increases in maximal treadmill walking time (3.44 minutes, $P < .001$), walking impairment distance score (10.7, $P = .02$), and SF-36PF score (7.5, $P = .02$). The resistance training group had greater increases in maximal treadmill walking time (1.9 minutes, $P = .009$), walking impairment scores for distance (6.92, $P = .02$), stair climbing (10.4, $P = .03$), and SF-36PF score (7.5, $P = .04$) than controls.

Comment: This study indicates that patients with PAD without symptoms of claudication should be treated with supervised treadmill exercise to improve function and, as suggested by improvements in brachial artery flow–mediated dilatation, improve underlying endothelial dysfunction that may contribute to atherosclerosis. Supervised treadmill exercise produces greater increases in 6-minute walk performance than resistance training. Resistance training, however, also produced potential clinical improvements on quality of life measures and stair climbing ability. It is becoming increasingly clear that patients with PAD, whether or not they are symptomatic, should be treated essentially as low-level, deconditioned athletes. Benefits can be measured from both resistance and nonresistance training that may over time reduce the accelerated functional decline associated with PAD.

Von Willebrand Factor, Type 2 Diabetes Mellitus, and Risk of Cardiovascular Disease: The Framingham Offspring Study

Frankel DS, Meigs JB, Massaro JM, et al. Circulation 2008;118:2533-9.

Conclusion: Increased levels of von Willebrand factor (vWF) are associated with the risk of cardiovascular disease in patients with insulin resistance or type 2 diabetes mellitus.

Summary: vWF is a large glycoprotein produced by endothelial cells that participates in the initial steps of thrombus formation by mediating platelet adhesion to injured endothelium. Because it interacts with endothelium, vWF may be a biomarker of endothelial damage. Because vWF is also known to be associated with insulin resistance and type 2 diabetes, vWF may be a risk factor for cardiovascular disease and may have increased significance in patients with insulin resistance or type 2 diabetes.

The authors tested the hypothesis that vWF predicted the incidence cardiovascular disease in 3799 Framingham Offspring Study participants, focusing on those with insulin resistance or type 2 diabetes. The Framingham Offspring Study is a prospective observational study of cardiovascular disease and risk factors. It began in 1971 by enrolling children of the original Framingham Heart Study cohort and the children's spouses. During 11 years of follow-up, cardiovascular disease developed in 351 participants. Adjusting for age, sex, blood pressure, smoking, body mass index, and high-density lipoprotein levels as well as treatment with aspirin, insulin, antihypertensives, and lipid-lowering medications, the hazard ratio (HR) for cardiovascular disease was 0.94 in the second quartile of vWF distribution, 0.98 in the third quartile, and 1.32 in the highest quartile, using the lowest quartile as the reference ($P = .04$ for trend). Adjusting for type 2 diabetes or insulin resistance attenuated the association (HRs for top quartile 1.28, and 1.21, respectively). The model was also stratified for diabetes and insulin resistance distribution (top quartile vs lower three quartiles). vWF was associated with cardiovascular disease among participants with diabetes mellitus (HR for top quartile relative to bottom, 1.47; $P = .04$) but not among nondiabetic participants (HR, 1.15; $P = .5$). vWF was also associated with cardiovascular disease among those with insulin resistance (HR, 1.5; $P = .01$) but not among those who were insulin sensitive (HR, 1.02; $P = .9$).

Comment: The data suggest vWF may be a risk factor unique in patients with type 2 diabetes mellitus or insulin resistance. Although diabetes mellitus and insulin resistance are clear risk factors for cardiovascular disease, patients with these risk factors have varying severities of clinical manifestations of atherosclerosis. This study offers the possibility of additional risk stratification among these patients based on levels of vWF.